

AMENDEMENTS TO THE CLAIMS

Claims 1-9 (Canceled)

Claims 10-13 (Withdrawn)

Claims 14-19 (Canceled)

Claims 20-24 (Withdrawn)

25. (New) A transgenic mouse whose genome comprises a disruption in an endogenous PKDL2 gene, wherein where the disruption is homozygous, the transgenic mouse lacks production of functional PKDL2 protein, and exhibits increased activity, relative to a wild-type control mouse.

26. (New) The transgenic mouse of claim 25, wherein the increased activity is characterized by an increase in total distance traveled in an open field environment, relative to a wild-type control mouse.

27. (New) A cell or tissue obtained from the transgenic mouse of claim 25.

28. (New) A transgenic mouse comprising a heterozygous disruption in an endogenous PKDL2 gene, wherein the disruption in a homozygous state inhibits production of functional PKDL2 protein resulting in a transgenic mouse exhibiting increased activity, relative to a wild-type control mouse.

29. (New) The transgenic mouse of claim 28, wherein the increased activity is characterized by an increase in total distance traveled in an open field environment, relative to a wild-type control mouse.

30. (New) A method of producing a transgenic mouse comprising a disruption in an endogenous PKDL2 gene, the method comprising:

(a) introducing a targeting construct capable of disrupting endogenous PKDL2 gene into a murine embryonic stem cell;

(b) introducing the murine embryonic stem cell into a mouse blastocyst;

(c) implanting the resulting blastocyst into a pseudopregnant mouse, wherein the pseudopregnant mouse gives birth to a chimeric mouse; and

(d) breeding the chimeric mouse to produce the transgenic mouse, wherein where the disruption is homozygous, the transgenic mouse lacks production of functional PKDL2 protein and exhibits increased activity, relative to a wild-type control mouse.

31. (New) The transgenic mouse produced by the method of claim 30.

32. (New) A targeting construct comprising:

- (a) a first polynucleotide sequence homologous to at least a first portion of an endogenous PKDL2 gene;
- (b) a second polynucleotide sequence homologous to at least a second portion of the endogenous PKDL2 gene; and
- (c) a selectable marker gene located between the first and second polynucleotide sequences;

wherein the targeting construct, when introduced into a murine embryonic stem cell, leads to the production of a transgenic mouse comprising a disruption in an endogenous PKDL2 gene, wherein where the disruption is homozygous, the transgenic mouse lacks production of functional PKDL2 protein and exhibits, relative to a wild-type mouse, increased activity.

33. (New) A murine embryonic stem cell comprising a disruption in an endogenous PKDL2 gene, the disruption produced using the targeting construct of claim 32.

34. (New) A method of producing a targeting construct, the method comprising:

- (a) providing a first polynucleotide sequence homologous to at least a first portion of an endogenous murine PKDL2 gene;
- (b) providing a second polynucleotide sequence homologous to at least a second portion of the endogenous murine PKDL2 gene;
- (c) providing a selectable marker gene; and
- (d) inserting the first sequence, second sequence, and selectable marker gene into a vector such that the selectable marker gene is located between the first and second sequences to produce the targeting construct,

wherein the targeting construct, when introduced into a murine embryonic stem cell, leads to the production of a transgenic mouse comprising a disruption in an endogenous PKDL2 gene, wherein where the disruption is homozygous, the transgenic mouse lacks production of functional PKDL2 protein and exhibits, relative to a wild-type mouse, increased activity.